§ 440.36a Sterile methicillin sodium monohydrate.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Methicillin sodium monohydrate is the monohydrated sodium salt of (2,6-dimethoxyphenyl) penicillin. It is so purified and dried that:

(i) It contains not less than 815 micrograms of methicillin per milligram.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not less than 3 percent and not more than 6 percent.

(vi) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 5.0 and not more than 7.5.

(vii) Its methicillin content is not less than 81.5 percent.

(viii) It is crystalline.

(ix) It passes the identity test.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this subchapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this subchapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, moisture, pH, methicillin content, crystallinity, and identity.

(ii) Samples required:

(*a*) For all tests except sterility: 10 packages, each containing approximately 300 milligrams, plus one package containing approximately 2 grams.

(*b*) For sterility testing: 20 packages, each containing approximately 600 milligrams.

(b) *Tests and methods of assay*—(1) *Potency*. Use any of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(i) *Microbiological agar diffusion assay*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed portion of the sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 10 micrograms of methicillin per milliliter (estimated).

(ii) *Iodometric assay*. Proceed as directed in § 436.204 of this subchapter.

(iii) *Hydroxylamine colorimetric assay*. Proceed as directed in § 436.205 of this subchapter.

(2) *Sterility*. Proceed as directed in in § 436.20 of this subchapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(a) of this chapter, using a solution containing 60 milligrams of methicillin per milliliter.

(4) [Reserved]

(5) *Moisture.* Proceed as directed in § 436.201 of this subchapter.

(6) *pH*. Proceed as directed in § 436.202 of this subchapter, using an aqueous solution containing 10 milligrams per milliliter.

(7) *Methicillin content.* Dissolve an accurately weighed portion of the sample in a sufficient accurately measured volume of distilled water to obtain a concentration of 0.2 milligram of methicillin per milliliter (estimated). Treat a portion of the methicillin working standard in the same manner. Using a suitable spectrophotometer equipped with a 1-centimeter quartz cell and distilled water as the blank, determine the absorbance at 280 nanometers. If a recording spectrophotometer is used, record the ultraviolet absorption spectrum from 250 nanometers to 300 nanometers. If a nonrecording spectrophotometer is used, determine the absorbance (on a solution containing 10 milligrams per 100 milliliters) at the 280-nanometer absorption peak. (The exact position of the peak should be determined for the particular instrument used.) Calculate as follows:

$$\text{Percent methicillin} = \frac{\text{Absorbance of sample} \times \text{weight of working standard} \times \text{volume of sample solution} \times \text{percent methicillin in working standard}}{\text{Absorbance of standard} \times \text{weight of sample} \times \text{volume of standard solution}}$$

(8) *Crystallinity.* Proceed as directed in § 436.203(a) of this subchapter.

(9) *Identity.* Using the sample solution prepared as described in paragraph (b)(7) of this section, determine the absorbancies at the absorption maximum at 280 nanometers and at the absorption minimum at 264 nanometers. The ratio of the two

$$A280/A264$$

should be not less than 1.30 and not more than 1.45.

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§ 440.37a Sterile mezlocillin sodium monohydrate.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Sterile mezlocillin sodium monohydrate is the monohydrate sodium salt of (2*S*, 5*R*, 6*R*)-3,3-dimethyl-6-[(*R*)-2-[3-(methylsulfonyl)-2-oxo-1-imidazolidine-carboxamido]-2-phenylacetamido]-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid. It is so purified and dried that:

(i) It contains not less than 838 micrograms and not more than 978 micrograms of mezlocillin per milligram on an anhydrous basis. If it is packaged for dispensing, its mezlocillin content is not less than 90 percent and not more than 115 percent of the number of milligrams of mezlocillin that it is represented to contain.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not more than 6.0 percent.

(vi) Its pH in an aqueous solution containing 100 milligrams per milliliter is not less than 4.5 and not more than 8.0.

(vii) The specific rotation in an aqueous solution containing 10 milligrams of mezlocillin per milliliter at 25° C is 185°±10°.

(viii) It gives a positive identity test for mezlocillin.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, moisture, pH, specific rotation, and identity.

(ii) Samples required:

(*a*) If it is packaged for repacking or for use in the manufacture of another drug:

(*1*) For all tests except sterility: 10 packages, each containing approximately 300 milligrams; and 5 packages, each containing approximately 1 gram.

(*2*) For sterility testing: 20 packages, each containing approximately 300 milligrams.

(*b*) If it is packaged for dispensing:

(*1*) For all tests except sterility: A minimum of 15 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Use either of the following methods; however, the results obtained from the hydroxylamine colorimetric assay shall be conclusive.

(i) *Hydroxylamine colorimetric assay.* Proceed as directed in § 442.40(b)(1)(ii) of this chapter, except:

(*a*) *Buffer.* In lieu of the buffer described in § 442.40(b)(1)(ii)(*b*)(*2*) of this chapter, use the buffer prepared as follows: Dissolve 200 grams of primary standard tris (hydroxymethyl) aminomethane in sufficient distilled water to make 1 liter. Filter before use.

(*b*) *Preparation of working standard solution.* Dissolve and dilute an accurately weighed portion of the